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New discovery points the way towards malaria 'vaccine'

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Malaria kills anywhere from one to three million people around the world annually and affects the lives of up to 500 million more. Yet until now, scientists did not fully understand exactly how the process that caused the disease's severe hallmark fevers began.

A team led by Dr. Martin Olivier from the Research Institute of the McGill University Health Centre (RI-MUHC) and McGill University in Montreal has solved this mystery, and may have blazed a trail towards the development of vaccine-like treatments to limit the severity of the devastating parasitic ailment. The results of their study will be published August 21 in the journal *PLoS Pathogens*.

Malaria is a mosquito-borne infectious disease spread by parasites from the Plasmodium family. Inside the human body, the malaria parasite infects red blood cells where it survives and reproduces by feeding on the cells' contents. Eventually the cells burst, releasing the parasites and also a waste byproduct of their reproductive process: hemozoin.

Researchers at the RI-MUHC and McGill University, discovered that hemozoin, a crystal-like substance may be the missing link that explains why malaria leads to devastating inflammation and fever.

"Our results describe the mechanism by which the hemozoin activates the immune system, resulting in the production of inflammation mediators and in the high fever that we witness in malaria patients," said study first-author Dr. Marina Tiemi Shio of the RI-MUHC.

Hemozoin is first ingested by 'cleaning' cells called macrophages, explained the researcher which leads to a chain reaction ending in the activation of the inflammasome: an important structure inside immune cells which lead to inflammation. Activation of the inflammasome produces the body's fever mediator, interleukin beta (IL-beta).

"Our work is a milestone in that it is the first study that reveals the enzymes that act as intermediary between the hemozoin and inflammasome," explained Dr. Olivier. "Now our picture of the process that goes from infection to fever is more or less complete."

"On the other hand we also proved that malaria is too complex to be narrowed down to one single mechanism," he continued. "In the absence of either IL-beta or a functional inflammsaome, the development of the disease is delayed but not completely stopped. Although the discovery of this relationship is important, there are other mechanisms at work."

The mechanisms that go from the activation of the inflammasome to the onset of the malaria symptoms were already familiar to scientists, but until now the beginning of the process was unknown.

"These results prove the primary role hemozoin plays in the development of malaria, and designates it as a favoured choice for future innovative treatments," added Dr. Olivier.

The researchers believe it will be possible to familiarize the immune system to small quantities of hemozoin and diminish the inflammatory response in the event of infection, according to a principle similar to that of vaccines.

Source: McGill University (news : web)